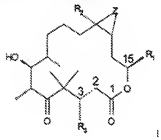
Amendments to the Claims

This Listing of the Claims will replace all prior versions, and listings, of claims in the application.

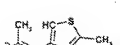
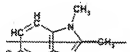
Listing of the Claims:

1. (Currently Amended) A compound of formula I



I

~~Wherein~~ wherein

R_1 is ~~selected from: a)~~  ~~and b)~~  ;

R_2 is lower alkyl or hydrogen;

R_3 is ~~OH or~~ hydrogen;

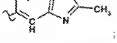
Z is O, C or -Z- is a bond between the two binding carbon atoms;

is a single or double bond between C2 and C3;

or salts thereof;

~~with the proviso that when R1 is a, R3 is hydrogen and that when R1 is b, Z is O or a bond, and R2 is methyl R3 is not OH.~~

2. (Currently Amended) A The compound of formula I according to claim 1, wherein

R_1 is  ;

R_2 is lower alkyl; ~~preferably methyl~~

Author Search

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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 25 Jan 2010  VOL 152 ISS 5
FILE LAST UPDATED: 24 Jan 2010  (20100124/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Oct 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Oct 2009

HCAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2009.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate
substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> D STAT QUE L11
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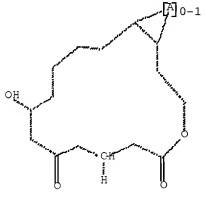


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L6              STR
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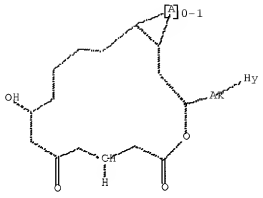

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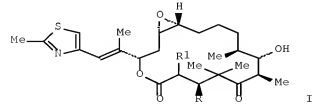
=> D IBIB ED ABS HITSTR L11 1-3

L11 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER:	2008:191355 HCAPLUS Full-text
DOCUMENT NUMBER:	148:355544
TITLE:	Conformational Preferences of Natural and C3-Modified Epothilones in Aqueous Solution
AUTHOR(S):	Erdelyi, Mate; Pfeiffer, Bernhard; Hauenstein, Kurt; Fohrer, Joerg; Gertsch, Juerg; Altmann, Karl-Heinz; Carlomagno, Teresa
CORPORATE SOURCE:	NMR-Based Structural Biology, Max-Planck-Institute for Biophysical Chemistry, Goettingen, D-37077, Germany
SOURCE:	Journal of Medicinal Chemistry (2008), 51(5), 1469-1473 CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER:	American Chemical Society
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 148:355544
ED Entered STN:	15 Feb 2008

GI



I

AB The conformational properties of the microtubule-stabilizing agent epothilone A (I, R = OH, R1 = H) and its 3-deoxy and 3-deoxy-2,3-didehydro derivs. I (R = R1 = H) and I (RR1 = E-bond) have been investigated in aqueous solution by a combination of NMR spectroscopic methods, Monte Carlo conformational searches, and NAMFIS calcns. The tubulin-bound conformation of epothilone A, as previously proposed on the basis of solution NMR data, was found to represent a significant fraction of the ensemble of conformations present for the free ligands in aqueous solution

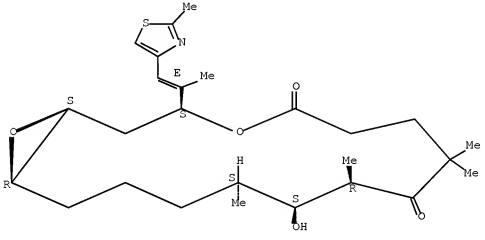
IT 1012306-80-7P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(conformational preferences of epothilone A and 3-deoxy derivs. in aqueous solution and antitumor activity)

RN 1012306-80-7 HCAPLUS

CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 11-hydroxy-8,8,10,12-tetramethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,10R,11S,12S,16R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2005:1305128 HCAPLUS Full-text

DOCUMENT NUMBER: 144:170808

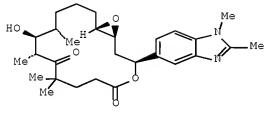
TITLE: Scaffolds for microtubule inhibition through extensive modification of the epothilone template

AUTHOR(S): Cachoux, Frederic; Isarno, Thomas; Wartmann, Markus; Altmann, Karl-Heinz

CORPORATE SOURCE: Department of Chemistry and Applied Biosciences Institute of Pharmaceutical Sciences, ETH Honggerberg, Zurich, 8093, Switz.

SOURCE: Angewandte Chemie, International Edition (2005), 44(45), 7469-7473

CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:170808
ED Entered STN: 14 Dec 2005
GI



I

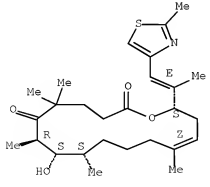
AB The microtubule-stabilizing agent I was obtained through extensive modification of the structure of natural epothilone. Despite these structural differences, the biol. potency of I is comparable with that of epothilone A and taxol.

IT 865535-36-0P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation, microtubule-stabilizing and antitumor activity of epothilone analogs)

RN 865535-36-0 HCAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 8-hydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (7R,8S,9S,13Z,16S)- (CA INDEX NAME)

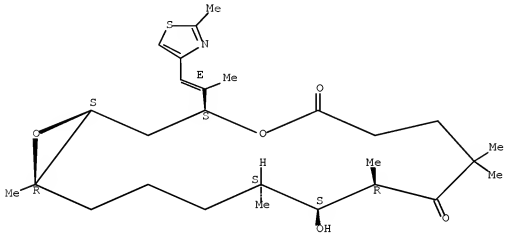
Absolute stereochemistry.
Double bond geometry as shown.



IT 865535-37-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL

(Biological study); PREP (Preparation)
(preparation, microtubule-stabilizing and antitumor activity of epothilone analogs)
RN 865535-37-1 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 11-hydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,10R,11S,12S,16R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



OS.CITING REF COUNT: 19 THERE ARE 19 CAPLUS RECORDS THAT CITE THIS RECORD (19 CITINGS)
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2005:1042238 HCAPLUS Full-text
DOCUMENT NUMBER: 143:346984
TITLE: Preparation of epothilone derivatives
INVENTOR(S): Altmann, Karl-Heinz
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005090335	A1	20050929	WO 2005-EP2756	20050315
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,				

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     AU 2005223325          B2    20090910
     CA 2556915             A1    20050929    CA 2005-2556915         20050315
     EP 1730138             A1    20061213    EP 2005-716085          20050315
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     CN 1926133             A     20070307    CN 2005-80006931        20050315
     BR 2005008874          A     20070904    BR 2005-8874            20050315
     JP 2007529455          T     20071025    JP 2007-503276          20050315
     MX 2006010415          A     20061110    MX 2006-10415           20060912
     KR 2007006773          A     20070111    KR 2006-718936          20060915
     IN 2006CN03364         A     20070706    IN 2006-CN3364          20060915
     US 20080114040         A1    20080515    US 2007-591921          20070530
PRIORITY APPLN. INFO.:                         GB 2004-5898         A  20040316
                                               WO 2005-EP2756       W  20050315
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S):         CASREACT 143:346984; MARPAT 143:346984
ED   Entered STN:  29 Sep 2005
GI
```

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

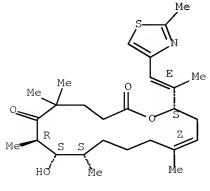
AB Epothilone derivs. I (R1 = Q, Q1; R2 = H, alkyl; R3 = OH, H; Z = O, C; bond between C2 and C3 may be single or double) were prepared as antitumor agents. Thus, the epothilone II was prepared via coupling of III with IV followed by hydrolysis, cyclization and deprotection. The proliferation inhibition (IC50) of II towards KB-31 cell lines was 54.9 nmol-1.

IT 865535-36-0P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of epothilone derivs.)

RN 865535-36-0 HCAPLUS

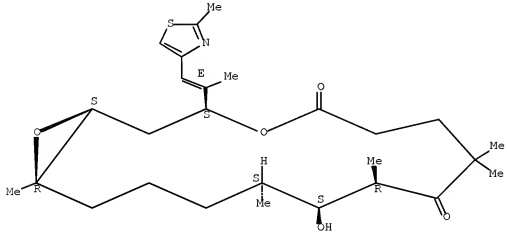
CN Oxacyclohexadec-13-ene-2,6-dione, 8-hydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (7R,8S,9S,13Z,16S)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT 865535-37-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of epothilone derivs.)
RN 865535-37-1 HCAPLUS
CN 4,17-Dioxabicyclo[14.1.0]heptadecane-5,9-dione, 11-hydroxy-8,8,10,12,16-pentamethyl-3-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1S,3S,10R,11S,12S,16R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Structure Search

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FILE COVERS 1907 - 25 Jan 2010  VOL 152 ISS 5
FILE LAST UPDATED: 24 Jan 2010  (20100124/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Oct 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Oct 2009

HCAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2009.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate
substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> D STAT QUE L9
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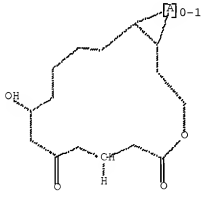


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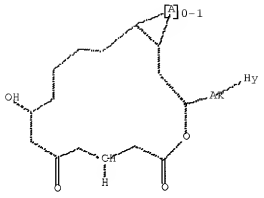


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L17            1 L9 NOT L11

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FILE CONTENT: 1961-PRESENT VOL 152 ISS 5 (20100124/ED)

MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US  20090312360 17 DEC 2009
DE 102008025751 03 DEC 2009
EP      2128165 02 DEC 2009
JP   2009286787 10 DEC 2009
WO   2009148961 10 DEC 2009
GB      2460460 02 DEC 2009
FR      2931669 04 DEC 2009
RU      2375416 10 DEC 2009
CA      2638573 30 OCT 2009

The new MARPAT User Guide is now available at:
 http://www.cas.org/support/stngen/stndoc/marpat.html.

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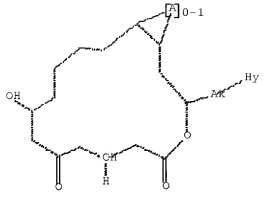


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Structure attributes must be viewed using STN Express query preparation.
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PROCESSING COMPLETED FOR L17
PROCESSING COMPLETED FOR L16
L18          11 DUP REM L17 L16 (0 DUPLICATES REMOVED)
                ANSWER '1' FROM FILE HCAPLUS
                ANSWERS '2-11' FROM FILE MARPAT

=> D IBIB ED ABS HITSTR 1; D IBIB AB QHIT 2-11

L18  ANSWER 1 OF 11  HCAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:         2006:151056  HCAPLUS  Full-text
DOCUMENT NUMBER:          144:247167
TITLE:                    Epothilone analogs as therapeutic agents for the
                          treatment of abnormal cellular proliferation diseases
INVENTOR(S):              Snyder, James P.; Nettles, James; Liotta, Dennis C.;
                          Kingston, David George Ian; Thota, Ganesh
PATENT ASSIGNEE(S):       Emory University, USA; Virginia Polytechnic Institute
                          and State University
SOURCE:                   PCT Int. Appl., 239 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006017761	A2	20060216	WO 2005-US27942	20050805
WO 2006017761	A3	20060615		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-599197P P 20040805

OTHER SOURCE(S): MARPAT 144:247167

ED Entered STN: 17 Feb 2006

AB Epothilone analogs are provided which are useful as microtubule stabilizing agents and in the treatment of abnormal cellular proliferation diseases and disorders are disclosed. Methods of making the compds., compns. containing the compds., 3D binding models of the binding of epothilone analogs on α,β-tubulin, and methods for its use in predicting, designing, or selecting therapeutically useful epothilone analogs are also provided.

IT 876124-44-6 876124-45-7 876124-46-8

RL: PRP (Properties)

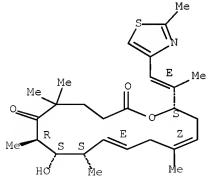
(epothilone analogs as therapeutic agents for treatment of abnormal cellular proliferation diseases)

RN 876124-44-6 HCAPLUS

CN Oxacyclohexadeca-10,13-diene-2,6-dione, 8-hydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (7R,8S,9S,10E,13Z,16S)- (CA INDEX NAME)

Absolute stereochemistry.

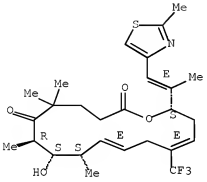
Double bond geometry as shown.



RN 876124-45-7 HCAPLUS

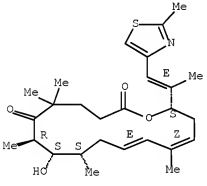
CN Oxacyclohexadeca-10,13-diene-2,6-dione, 8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-(trifluoromethyl)-, (7R,8S,9S,10E,13E,16S)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 876124-46-8 HCAPLUS
CN Oxacyclohexadeca-11,13-diene-2,6-dione, 8-hydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (7R,8S,9S,11E,13Z,16S)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 11 MARPAT COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 143:346984 MARPAT Full-text
TITLE: Preparation of epothilone derivatives
INVENTOR(S): Altmann, Karl-Heinz
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 68 pp.

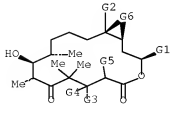
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005090335	A1	20050929	WO 2005-EP2756	20050315
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005223325	A1	20050929	AU 2005-223325	20050315
AU 2005223325	B2	20090910		
CA 2556915	A1	20050929	CA 2005-2556915	20050315
EP 1730138	A1	20061213	EP 2005-716085	20050315
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 1926133	A	20070307	CN 2005-80006931	20050315
BR 2005008874	A	20070904	BR 2005-8874	20050315
JP 2007529455	T	20071025	JP 2007-503276	20050315
MX 2006010415	A	20061110	MX 2006-10415	20060912
KR 2007006773	A	20070111	KR 2006-718936	20060915
IN 2006CN03364	A	20070706	IN 2006-CN3364	20060915
US 20080114040	A1	20080515	US 2007-591921	20070530
PRIORITY APPLN. INFO.:			GB 2004-5898	20040316
			WO 2005-EP2756	20050315

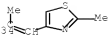
OTHER SOURCE(S): CASREACT 143:346984

AB Epothilone derivs. I (R1 = Q, Q1; R2 = H, alkyl; R3 = OH, H; Z = O, C; bond between C2 and C3 may be single or double) were prepared as antitumor agents. Thus, the epothilone II was prepared via coupling of III with IV followed by hydrolysis, cyclization and deprotection. The proliferation inhibition (IC50) of II towards KB-31 cell lines was 54.9 nmol-1.

MSTR 1



G1 = 34



G6 = bond
Patent location: claim 1
Note: or salts
Note: substitution is restricted

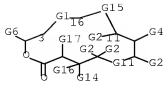
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 11 MARPAT COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 140:163628 MARPAT Full-text
TITLE: Method for the asymmetric synthesis of epothilones and epothilone analogs
INVENTOR(S): White, James David; Sundermann, Kurt Frederick; Carter, Rich Garrett
PATENT ASSIGNEE(S): Oregon State University, USA; State of Oregon Acting by and Through The State Board of Higher Education On Behalf of Oregon State University
SOURCE: U.S. Pat. Appl. Publ., 36 pp., Cont.-in-part of U.S. Ser. No. 846,154.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040030147	A1	20040212	US 2003-354694	20030129
US 6906188	B2	20050614		
US 20020062030	A1	20020523	US 2001-846154	20010430
US 6596875	B2	20030722		
PRIORITY APPLN. INFO.:			US 2001-846154	20010430
			US 1999-118883P	19990205
			US 2000-499596	20000207

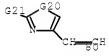
AB A method for the preparation of epothilones and analogs, such as I (R = H, alkyl, protecting group; R1 = aryl; R2 = H, alkyl; R3 = H, alkyl, R4CO, R4OCO, R4SO2; R4 = H, alkyl, aryl; X, Y = O, NH, S, CO, C) is described. Embodiments of the method provide convenient access to analogs of the epothilones, such as those having alternate stereochem. and those containing an ester, amide, thioester, or alkyne moieties in the macrocycle. One embodiment of the method was used to synthesize epothilone B by a convergent approach that entailed Wittig coupling of an ylide derived from phosphonium bromide with an aldehyde. Macrolactonization of a resulting hydroxy acid provided an intermediate diene epothilone analog which upon selective saturation of the 9,10-olefin and subsequent epoxidn. provided epothilone B. Epothilone B exhibits microtubule stabilization and has IC50 values ranging from 0.32-0.16 nM in a variety of human cancer cell lines.

MSTR 1



G1 = 21-3 22-16

G4 = OH
G6 = 80



G11 = C(O)
G15 = CH2CH2
G20 = O
Patent location: claim 1

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 11 MARPAT COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 138:24591 MARPAT Full-text
TITLE: Preparation of epothilone derivatives for therapeutic use as anti-cancer agents
INVENTOR(S): Regueiro-Ren, Alicia; Borzilleri, Robert M.; Vite, Gregory D.; Kim, Soong-Hoon
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002098868	A1	20021212	WO 2002-US15397	20020514

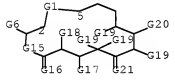
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,

UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2449077	A1	20021212	CA 2002-2449077	20020514	
AU 2002309843	A1	20021216	AU 2002-309843	20020514	
US 20030087888	A1	20030508	US 2002-144879	20020514	
US 6800653	B2	20041005			
EP 1392664	A1	20040303	EP 2002-736867	20020514	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004532888	T	20041028	JP 2003-501991	20020514	
MX 2003010909	A	20040217	MX 2003-10909	20031127	
PRIORITY APPLN. INFO.:			US 2001-295499P	20010601	
			WO 2002-US15397	20020514	

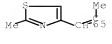
AB Epothilone derivs., such as I [B1 = H, OH, alkoxy, acyloxy, carbamoyl, etc.; W = O, S, NR16; X = O, S, CO, SO, SO2, CH2, CC12, CBr2, NR1, etc.; R1 = H, alkyl; R16 = H, alkyl, aryl, cycloalkyl, heterocyclyl, etc.], were prepared for use as antitumor agents. Thus, aza-epothilone derivative II via a series of synthetic steps which included epoxidn. of epothilone C using 0.0004 M Na2EDTA, F3CCOMe, 2KHSO5.KHSO4.K2SO4 (potassium peroxymonosulfate) and NaHCO3 in MeCN to form epothilone A and 12,13-diepi-epothilone A in 57 and 29% yields, resp., followed by epoxide ring opening/azidation of 12,13-diepi-epothilone A using NaN3 and NH4Cl in EtOH to form the azido-hydroxy derivative in 59% yield, and, finally, formation of II in 62% yield using PPh3 and heating the azido-hydroxy derivative at 60° for 14 h. in THF. The prepared epothilone derivs. were assayed in vitro for their effect on tubulin polymerization and for cytotoxicity against HCT-116 human colon carcinoma cells.

MSTR 1



G1 = 3-2 4-5

G6 = 65



G15 = O
G16 = O
G20 = 74

G21 = O
Patent location: claim 1
Note: and salts, solvates, or hydrates

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 11 MARPAT COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 137:129901 MARPAT Full-text
TITLE: Pharmaceutical dosage forms of epothilones for oral administration
INVENTOR(S): Bandyopadhyay, Rebanta; Malloy, Timothy M.; Panaggio, Andrea; Raghavan, Krishnaswamy Srinivas; Varia, Sailesh Amilal
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002058701	A1	20020801	WO 2002-US2518	20020125
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2681962	A1	20020801	CA 2002-2681962	20020122
NZ 526871	A	20060127	NZ 2002-526871	20020122
CN 101112373	A	20080130	CN 2007-10142237	20020122
EP 1938821	A2	20080702	EP 2008-152923	20020122
EP 1938821	A3	20090218		
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, TR, AL, LT, LV, MK, RO, SI				
CA 2434584	A1	20020801	CA 2002-2434584	20020125
AU 2002253880	A1	20020806	AU 2002-253880	20020125
AU 2002253880	B2	20061109		
US 20020177615	A1	20021128	US 2002-57390	20020125
US 6576651	B2	20030610		
EE 200300329	A	20031015	EE 2003-329	20020125
EP 1361877	A1	20031119	EP 2002-723073	20020125
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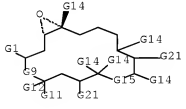
HU	2003003800	A2	20040329	HU 2003-3800	20020125
HU	2003003800	A3	20050228		
BR	2002006695	A	20040420	BR 2002-6695	20020125
CN	1498106	A	20040519	CN 2002-806992	20020125
CN	1268336	C	20060809		
JP	2004528287	T	20040916	JP 2002-559035	20020125
TW	250017	B	20060301	TW 2002-91101287	20020125
RU	2291695	C2	20070120	RU 2003-126174	20020125
IN	2003MN00670	A	20050211	IN 2003-MN670	20030702
MX	2003006476	A	20030922	MX 2003-6476	20030718
NO	2003003343	A	20030924	NO 2003-3343	20030724
BG	108027	A	20041230	BG 2003-108027	20030724
US	40387	E1	20080617	US 2005-149501	20050609
US	20060013836	A1	20060119	US 2005-226017	20050914
US	20090069393	A1	20090312	US 2008-264375	20081104

PRIORITY APPLN. INFO.:

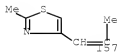
US	2001-264228P 20010125
US	2001-290019P 20010511
US	2001-290006P 20010511
US	2001-290008P 20010511
US	2002-51727 20020117
CA	2002-2434526 20020122
CN	2002-804090 20020122
EP	2002-713446 20020122
US	2002-57390 20020125
WO	2002-US2518 20020125
US	2005-226017 20050914

AB The invention relates to methods of increasing the bioavailability of orally administered epothilones. Epothilones administered by the methods of the invention are sufficiently bioavailable to have a pharmacol. effect. The stability of an analog of epothilone in 80:20 propylene glycol–EtOH was evaluated by reconstituting 25 mg analog with 80:20 propylene glycol–EtOH to provide a liquid oral dosage form at concns. of 2.5–12.5 mg/mL. The resulting liquid oral dosage form was then stored up to 20 h at ambient temperature and room light and at refrigerated temperature No changes from initial were observed in the appearance of the liquid oral dosage form at either storage condition. An increase in total impurities/degradants and a decrease in potency were observed after storage at ambient temperature and room light for 20 h. A slight increase in total impurities/degradants was observed after 20 h storage at refrigerated temperature The change in total impurities was attributed to an increase of an oxazine impurity/degradant.

MSTR 1



G1 = 157



G9 = O
G15 = 102

G16 = O
G21 = OH
G11+G12= O
Patent location: claim 1
Note: or pharmaceutically acceptable salts, solvates, clathrates, hydrates or prodrugs

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 11 MARPAT COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 137:145575 MARPAT Full-text
TITLE: Pharmaceutical forms of epothilones for oral administration
INVENTOR(S): Bandyopadhyay, Rebanta; Malloy, Timothy M.; Panaggio, Andrea; Raghavan, Krishnaswamy Srinivas; Varia, Sailesh Amilal
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002058699	A1	20020801	WO 2002-US1693	20020122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2681962	A1	20020801	CA 2002-2681962	20020122
AU 2002241935	A1	20020806	AU 2002-241935	20020122
CN 101112373	A	20080130	CN 2007-10142237	20020122
EP 1938821	A2	20080702	EP 2008-152923	20020122
EP 1938821	A3	20090218		
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC,				

NL, PT, SE, TR, AL, LT, LV, MK, RO, SI

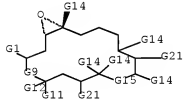
US 20020177615	A1	20021128	US 2002-57390	20020125
US 6576651	B2	20030610		
CN 1498106	A	20040519	CN 2002-806992	20020125
CN 1268336	C	20060809		
TW 250017	B	20060301	TW 2002-91101287	20020125
BG 108027	A	20041230	BG 2003-108027	20030724
US 40387	E1	20080617	US 2005-149501	20050609
US 20060013836	A1	20060119	US 2005-226017	20050914
US 20090069393	A1	20090312	US 2008-264375	20081104

PRIORITY APPLN. INFO.:

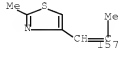
US 2001-264228P 20010125
US 2001-290019P 20010511
US 2001-290006P 20010511
US 2001-290008P 20010511
US 2002-51727 20020117
CA 2002-2434526 20020122
CN 2002-804090 20020122
EP 2002-713446 20020122
WO 2002-US1693 20020122
US 2002-57390 20020125
US 2005-226017 20050914

AB The invention relates to methods of increasing the bioavailability of orally administered epothilones in humans. Epothilones administered by the methods of the invention are sufficiently bioavailable to have a pharmacol. effect. The invention further relates to pharmaceutical compns., pharmaceutical dosage forms, and kits for use in the methods of the invention. A pharmaceutical kit for oral administration comprises (i) one or more epothilones and (ii) an acid neutralizing buffer containing dibasic sodium phosphate, sodium citrate, and citric acid, wherein the components are provided as compns. that can be reconstituted with a solvent to provide a liquid oral dosage form, or the sec. component is provided as a solid, e.g., a tablet, to be administered concurrently with or before administering epothilone solns. in propylene glycol/ethanol (80:20).

MSTR 1



G1 = 157



G9 = O
G15 = 102

G16 = O
G21 = OH
G11+G12= O
Patent location: claim 1
Note: or pharmaceutically acceptable salts, solvates, clathrates, hydrates or prodrugs

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

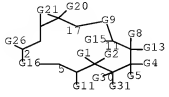
L18 ANSWER 7 OF 11 MARPAT COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 136:216592 MARPAT Full-text
TITLE: Procedures for the production of 12,13-cyclopropylepothilone derivatives, as well as for their use in pharmaceutical preparations
PATENT ASSIGNEE(S): Schering Ag, Germany
SOURCE: Ger. Offen., 64 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10041470	A1	20020228	DE 2000-10041470	20000818

PRIORITY APPLN. INFO.: DE 2000-10041470 20000818
OTHER SOURCE(S): CASREACT 136:216592
AB The present invention describes new 6-alkenyl- and 6-alkynylepothilone derivs., e.g., I [R1a, R1b = H, C1-10-alkyl, aryl, C7-20-aralkyl; R1aR1b = (CH2)r, CH2OCH2; r = 1 - 5; R2a = H, C1-10-alkyl, aryl, C7-20-aralkyl, (CH2)m-C.tplbond.C-(CH2)pR26, (CH2)m-C:C-(CH2)pR26, X1, X2; n = 0 - 5; p = 0 - 3; m = 0 - 4; R2b = (CH2)m-C.tplbond.C-(CH2)pR26, (CH2)m-C:C-(CH2)pR26, X1, X2; R3a = H, C1-10-alkyl, aryl, C7-20-aralkyl; R3b = O-protecting group; R4 = H, C1-10-alkyl, aryl, C7-20-aralkyl, halogen, OH, O-protecting group, CN; R5 = H, C1-10-alkyl, aryl, C7-20-aralkyl, (CH2)s-T; S = 1 - 4; T = OH, O-protecting group, halogen; R6R7 = C(R33)2, NR32 AY = OC(:O), OCH2, CH2C(:O), NR29C(:O), NR29SO2; DE = CH2CH2, CH2O, OCH2; G = X:CR8-, bicyclic or tricyclic aryl; X = O, (O-alkyl)2, etc.; Z = H, H,OH, H,O-protective group; R8 = H, halogen, CN, C1-20-alkyl, aryl, C7-20-aralkyl; R14 = H, OH, halogen, O-SO2-alkyl, O-SO2-aryl, O-SO2-aralkyl; R26 = H, C1-10-alkyl, aryl, C7-20-aralkyl, C1-10-acyl, OH, O-protecting group; R29 = H, C1-20-alkyl; R32 = H, C1-4-alkyl, C1-4-acyl; R33 = H, halogen], which interact with tubulins by stabilizing the formed microtubulins (no data). I are able specifically to affect cell division and are suitable, for example for the treatment of malignant tumors ovarial -, stomach -, colon -, adeno -, chest -, lungs -, head and neck carcinoma, malignant melanoma, acute lymphocytic and myelocytic leukemia. In addition I are suitable for the anti-angiogenesis therapy as well as for the treatment of chronic ignitable illnesses (psoriasis, arthritis). For the avoidance of uncontrolled cell rampant growths on as well as the better compatibility of medical implants I can be up and/or brought into polymers materials. According to invention, I can be used alone or for the achievement of additive

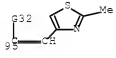
or synergistic effects in combination with further principles and substance classes applicable in the tumor therapy. Exptl. data from patents PCT/EP00/01333 and PCT/IB00/00657 are reproduced here.

MSTR 1A



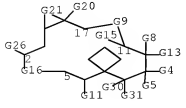
G9 = CH2CH2
G13 = OH
G16 = 51-2 52-5

G17 = C(O)
G26 = 95



G30+G31= O
Patent location: claim 1
Note: additional ring formation also claimed

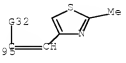
MSTR 1B



G9 = CH2CH2
G13 = OH

G16 = 51-2 52-5

G17 = C(O)
G26 = 95



G30+G31= O
Patent location: claim 1
Note: additional ring formation also claimed

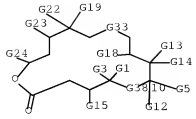
L18 ANSWER 8 OF 11 MARPAT COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 133:362656 MARPAT Full-text
TITLE: Preparation of 6-alkenyl-, 6-alkynyl- and 6-epoxyepothilone derivatives and their antitumor activity
INVENTOR(S): Klar, Ulrich; Schwede, Wolfgang; Skuballa, Werner; Buchmann, Bernd; Hoffmann, Jens; Lichtner, Rosemarie
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 298 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066589	A1	20001109	WO 2000-IB657	20000501
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19921086	A1	20001102	DE 1999-19921086	19990430
DE 19954228	A1	20010913	DE 1999-19954228	19991104
DE 10015836	A1	20011011	DE 2000-10015836	20000327
CA 2371226	A1	20001109	CA 2000-2371226	20000501
BR 2000010190	A	20020108	BR 2000-10190	20000501
EP 1173441	A1	20020123	EP 2000-922826	20000501
EP 1173441	B1	20090826		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO, CY, SE				
JP 2002543203	T	20021217	JP 2000-615619	20000501

JP 4024003	B2	20071219			
EE 200100568	A	20030217	EE 2001-568	20000501	
NZ 514989	A	20040227	NZ 2000-514989	20000501	
AU 772750	B2	20040506	AU 2000-43103	20000501	
SK 286858	B6	20090605	SK 2001-1551	20000501	
AT 440847	T	20090915	AT 2000-922826	20000501	
IN 2001MN01305	A	20070504	IN 2001-MN1305	20011019	
BG 106053	A	20020531	BG 2001-106053	20011026	
BG 65601	B1	20090227			
NO 2001005278	A	20011221	NO 2001-5278	20011029	
MX 2001011039	A	20030630	MX 2001-11039	20011030	
US 7125893	B1	20061024	US 2002-979939	20020606	
HK 1046681	A1	20080829	HK 2002-108204	20021113	
US 20050113429	A1	20050526	US 2004-965802	20041018	
US 7645891	B2	20100112			
IN 2005MN00837	A	20070608	IN 2005-MN837	20050802	
US 20060046997	A1	20060302	US 2005-214988	20050831	
PRIORITY APPLN. INFO.:			DE 1999-19921086	19990430	
			DE 1999-19954228	19991104	
			DE 2000-10015836	20000327	
			DE 2000-10013363	20000309	
			WO 2000-IB657	20000501	
			IN 2001-MN1305	20011019	
			US 2002-979939	20020606	

AB The antitumor agents, 6-alkenyl-, 6-alkynyl- and 6-epoxyepothilones I (R1a, R1b are same or different = H, C1-C10 alkyl, C6-C12 aryl, C7-C20 aralkyl each optionally substituted; or together = (CH2)m m = 1-5 or -CH2OCH2-; R2a(R2b replace a with b) = H, substituted alkyl, aryl, aralkyl, (CH2)ra-C.tplbond.(or =)C-(CH2)pa-R26a, Q, Q1 where n = 0-5; ra, rb = the same or different and = 0-4; pa, pb = the same or different and = 0-3; R3a = H, substituted alkyl, aryl or aralkyl; R3b = OH, OPG14; R14 = H, OR14a, halogen and R14a = H, SO2-alkyl, SO2-aryl or SO2-aralkyl; R4 = H, substituted alkyl, aryl or aralkyl, halogen, OR25, CN; R26a, R26b = same or different = H, substituted alkyl, aryl or aralkyl, C1-C10 acyl or if pa or pb > 0, addnl. a group OR27; R25 = R27 = R22 = H, PG; R5 = H, substituted alkyl, aryl or aralkyl, (CH2)sT s = 1-4, T = OR22 or halogen; R6, R7 = H or together = bond or O; G = X=CR8 or bi- or tricyclic aryl radical and R8 = H, halogen, CN, or substituted alkyl, aryl or aralkyl; X = O, two OR23 groups, C2-C10-alkylene-α,ω-dioxy straight chain or branched; H/OR9 or CR10R11 group and R23 = alkyl radical, R9 = H, PG, R10,R11 = same or different = H, substituted alkyl, aryl or aralkyl, or together with the methylene are a 5-7 carbocyclic ring; D-E = CH2CH2 or OCH2; A = OC(O), OCH2, CH2C(O), NR29C(O), NR29SO2 and R29 = H, alkyl; Z = O or H/OR12 and R12 = H, PG) were prepared Thus II was prepared in a multistep synthesis starting from (4S)-4-(2-methyl-1-oxoprop-2-yl)-2,2- dimethyl[1,3]dioxane and 5-trimethylsilylpent-4-in-1-yl magnesium bromide. II had an IC50 value [nM] of 3.0 for the growth inhibition of human MCF-7 breast- and 75 for multidrug resistant NCI/ADR carcinoma cell lines with a selectivity of 2.5. The new epothilone derivs. interact with tubulin by stabilizing microtubuli that are formed. They are able to influence the cell-splitting in a phase-specific manner and are therefore useful in treating diseases or conditions associated with the need for cell growth, division and/or proliferation. Thus the epothilone derivs. are suitable for treating malignant tumors, e.g., ovarian, stomach, colon, adeno-, breast, lung, head and neck carcinomas, malignant melanoma, acute lymphocytic and myelocytic leukemia; and for anti-angiogenesis therapy as well as for treatment of chronic inflammatory diseases (such as psoriasis, arthritis).

MSTR 1B



G14 = OH
G24 = 151

G33 = CH2
G38 = C(O)
G40 = alkyl <containing 1-4 C>
G41 = 156

Patent location: claim 1
Note: additional ring formation also claimed
Note: substitution is restricted

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

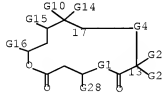
L18 ANSWER 9 OF 11 MARPAT COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 133:193025 MARPAT Full-text
TITLE: Preparation of new epothilone derivatives and their pharmaceutical uses
INVENTOR(S): Klar, Ulrich; Schwede, Wolfgang; Skuballa, Werner; Buchmann, Bernd; Schirner, Michael; Menrad, Andreas
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000049019	A2	20000824	WO 2000-EP1331	20000218

WO 2000049019 A3 20010301
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
DE 19908760 A1 20000824 DE 1999-19908760 19990218
PRIORITY APPLN. INFO.: DE 1999-19908760 19990218

AB Epothilone derivs. I (R1a, R1b = H, C1-C10 alkyl, aryl; C7-C20 aralkyl; or together are (CH2)m m = 1-5; or CH2OCH2; R2a, R2b = H, C1-C10 alkyl, aryl; C7-C20 aralkyl; or together are (CH2)n n = 2-5; G1-G-E-E1 = CR3aR3b-CR4=CH-CH2; CR3aR3b-CD(T)R4-CHD(T)-CH2; (2,3-epoxy)-CR3aR3b-CR4OCH-CH2; CR3aR3b-COH(H)R4-CHOH(H)-CH2; CR3a=CR4-CH=CH where R3a = H, C1-C10 alkyl, aryl; C7-C20 aralkyl; R14 = H, OR14a, halogen, OSO2R14b; R3b = OPG14 or R3b, R14a = bond; R4 = H, C1-C10 alkyl, aryl; C7-C20 aralkyl; R5 = H, C1-C10 alkyl, aryl; C7-C20 aralkyl, (CH2)s-A s = 1-4, A = OR22 or halogen; R22 = H or protecting group; R6, R7 = H, O, bond; R8 = H, C1-C10 alkyl, aryl; C7-C20 aralkyl; X = O, OR23, C2-C10-alkylene-α,ω-dihydroxy which can be a straight chain or branched; H/OR9 or the group CR10R11 where R23 = C1-C20 alkyl; R9 = H or a protecting group; R10,R11 = H, C1-C20 alkyl, aryl; C7-C20 aralkyl or R10,R11 together form a 5-7 membered carbocyclic ring; Y = O or 2 H atoms; Z = O or H/OR12 where R12 = H or a protecting group) were prepared in addition to all possible stereoisomers and mixts. Thus II was prepared from (±)-1-acetoxypentan-4-one in a multistep synthesis. These epothilone derivs. interact with tubulin by stabilizing the microtubuli which are formed. They are able to influence the cell division phase-specifically and are suitable for treating malignant tumors such as cancers of the ovaries, stomach, colon, glands, breasts, lungs, head and neck, malignant melanoma and acute lymphocytic and myelocytic leukemia. These compds. are also suitable for anti-angiogenesis therapy and for treating chronic inflammatory diseases (psoriasis, arthritis) and can be deposited on or in polymer materials in order to prevent uncontrolled cell proliferations on medical implants and to improve the compatibility. These derivs. can be used alone or in combination with other principles and classes of substances that can be used in the therapy of tumors to achieve additive or synergistic effects.

MSTR 1



G1 = 25

G4 = 19-17 12-13

G9 = OH (opt. substd.)
G16 = 109

G29 = 103

Patent location: claim 1
Note: additional substitution and ring formation also claimed
Stereochemistry: and stereoisomers and mixtures

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 10 OF 11 MARPAT COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 131:310502 MARPAT Full-text
TITLE: synthesis and cytotoxicity of 12,13-modified epothilone derivatives for use in treatment of tumors or other hyperproliferative cellular disease
INVENTOR(S): Vite, Gregory D.; Kim, Soong-Hoon Kim; Hofle, Gerhard
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9954319	A1	19991028	WO 1999-US7475	19990405

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP,

KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,
NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA,
UG, UZ, VN, YU, ZA, ZW
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA,
GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG

US 6380395	B1	20020430	US 1999-280192	19990329	
US 6399638	B1	20020604	US 1999-280191	19990329	
CA 2329181	A1	19991028	CA 1999-2329181	19990405	
AU 9934716	A	19991108	AU 1999-34716	19990405	
AU 748526	B2	20020606			
BR 9909795	A	20001226	BR 1999-9795	19990405	
TR 200003036	T2	20010122	TR 2000-3036	19990405	
EP 1073648	A1	20010207	EP 1999-916383	19990405	
EP 1073648	B1	20060920			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI, CY

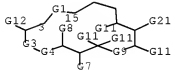
JP 2002512239	T	20020423	JP 2000-544658	19990405	
CN 1142923	C	20040324	CN 1999-805266	19990405	
EP 1589017	A2	20051026	EP 2005-15236	19990405	
EP 1589017	A3	20090422			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI, CY

AT 340777	T	20061015	AT 1999-916383	19990405	
PT 1073648	E	20061229	PT 1999-916383	19990405	
ES 2273484	T3	20070501	ES 1999-916383	19990405	
ES 2327803	T3	20091103	ES 1999-915273	19990405	
MX 2000010109	A	20010419	MX 2000-10109	20001016	
PRIORITY APPLN. INFO.:			US 1998-82564P	19980421	
			EP 1999-916383	19990405	
			WO 1999-US7475	19990405	

AB Synthesis and cytotoxicity of 12,13-modified epothilone derivs.(I) [R1 = H, (un)substituted alkyl; R2 = H if bond double or βOH if bond single; Y = O, NH; X = O, (un)substituted NH, OCH2, 2-methylthiazolo, S, (un)substituted CH2] is presented. Thus, I (R1 = H, X = NH, R2 = βOH, Y = O) (II) is prepared by epoxidn. of epothilone C followed by azidation and reductive imination. I are useful in treatment of tumors or other hyperproliferative cellular disease and show IC50 of 0.01-1000 nM in cell proliferation tests.

MSTR 1A



G1 = 16-3 18-15

G3 = O
G4 = 23

G5 = O
G9 = 31

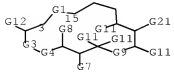
G12 = 50

G14 = 118

G21 = 213

G33 = O
Derivative: and salts, solvates or hydrates
Patent location: claim 1
Note: additional ring formation also claimed
Note: substitution is restricted

MSTR 1B



G1 = 16-3 18-15

G3 = O
G4 = 23

G5 = O
G9 = 31

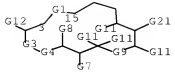
G12 = 50

G14 = 118

G21 = 213

G33 = O
Derivative: and salts, solvates or hydrates
Patent location: claim 1
Note: additional ring formation also claimed
Note: substitution is restricted

MSTR 1C



G1 = 16-3 18-15

G3 = O
G4 = 23

G5 = O
G9 = 31

G12 = 50

G14 = 118

G21 = 213

G33 = O
Derivative: and salts, solvates or hydrates
Patent location: claim 1
Note: additional ring formation also claimed
Note: substitution is restricted

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

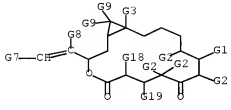
L18 ANSWER 11 OF 11 MARPAT COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 131:310501 MARPAT Full-text
TITLE: synthesis and cytotoxicity of 12,13-cyclopropane epothilone derivatives for use in treatment of tumors or other hyperproliferative cellular disease
INVENTOR(S): Vite, Gregory D.; Kim, Soong-Hoon Kim; Hofle, Gerhard
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9954318	A1	19991028	WO 1999-US7448	19990405
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG				
US 6380395	B1	20020430	US 1999-280192	19990329
US 6399638	B1	20020604	US 1999-280191	19990329
CA 2323609	A1	19991028	CA 1999-2323609	19990405
AU 9933827	A	19991108	AU 1999-33827	19990405
AU 757733	B2	20030306		
TR 200003036	T2	20010122	TR 2000-3036	19990405
EP 1073647	A1	20010207	EP 1999-915273	19990405
EP 1073647	B1	20090708		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
JP 2002512238	T	20020423	JP 2000-544657	19990405
CN 1142923	C	20040324	CN 1999-805266	19990405
EP 1589017	A2	20051026	EP 2005-15236	19990405
EP 1589017	A3	20090422		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
AT 340177	T	20061015	AT 1999-916383	19990405
PT 1073648	E	20061229	PT 1999-916383	19990405
ES 2273484	T3	20070501	ES 1999-916383	19990405
AT 435861	T	20090715	AT 1999-915273	19990405
ES 2327803	T3	20091103	ES 1999-915273	19990405
PRIORITY APPLN. INFO.:			US 1998-82564P	19980421
			EP 1999-916383	19990405
			WO 1999-US7448	19990405

AB Synthesis and cytotoxicity of 12,13-cyclopropane epothilone derivs. (I) [R1 = H, (un)substituted alkyl; R2 = H if bond double or βOH if bond single; R3 =

electron pair or =O; X = (un)substituted CH2] is presented. Thus, I (R1 = Me, R2 = OH on single bond, R3 = electron pair, X = CH2) (II) is prepared by converting epothilone B to epothilone D via deepoxidn. followed by alc. protection, cyclopropanation and desilylation. I are useful in treatment of tumors or other hyperproliferative cellular disease and show IC50 values of 0.01-1000 nM in cell proliferation tests.

MSTR 1



G1 = OH
G7 = 64

Derivative: or salts, solvates or hydrates
Patent location: claim 1

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Search History

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L1              STRUCTURE UPLOADED
                D
L2            0 SEA SSS SAM L1

     FILE 'HCAPLUS' ENTERED AT 08:35:33 ON 25 JAN 2010
                E US2007-591921/APPS
L3            1 SEA SPE=ON  ABB=ON  PLU=ON  US2007-591921/APPS
                D SCAN
                SEL RN

     FILE 'REGISTRY' ENTERED AT 08:36:41 ON 25 JAN 2010
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                -6/BI OR 865535-91-7/BI OR 865536-05-6/BI)
L5           14 SEA SSS FUL L1
L6              STRUCTURE UPLOADED
L7            1 SEA SUB=L5 SSS SAM L6
L8            6 SEA SUB=L5 SSS FUL L6

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L10         278 SEA SPE=ON  ABB=ON  PLU=ON  ALTMANN K?/AU
L11           3 SEA SPE=ON  ABB=ON  PLU=ON  L9 AND L10

     FILE 'WPIX' ENTERED AT 08:45:14 ON 25 JAN 2010
L12           0 SEA SSS SAM L6
L13           0 SEA SSS FUL L6

     FILE 'BEILSTEIN' ENTERED AT 08:46:16 ON 25 JAN 2010
L14           0 SEA SPE=ON  ABB=ON  PLU=ON  L8

     FILE 'MARPAT' ENTERED AT 08:46:24 ON 25 JAN 2010
L15           0 SEA SSS SAM L6
L16          10 SEA SSS FUL L6

     FILE 'HCAPLUS' ENTERED AT 08:48:18 ON 25 JAN 2010
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                D STAT QUE L9
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     FILE 'MARPAT' ENTERED AT 08:48:36 ON 25 JAN 2010
                D STAT QUE L16

     FILE 'HCAPLUS, MARPAT' ENTERED AT 08:48:51 ON 25 JAN 2010
L18           11 DUP REM L17 L16 (0 DUPLICATES REMOVED)
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